South African Appl. - 68/0962

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Patents Form No. 1A.

# REPUBLIC OF SOUTH AFRICA

## THE PATENTS ACT, 1952, AS AMENDED.

## APPLICATION FOR A PATENT UNDER INTERNATIONAL ARRANGEMENTS

(WITH AUTHORISATION OF AGENT)

Application No. 680962

FOR OFFICIAL USE ONLY

Filed 2-13-68

Ger. 2-14-67

Pub. 11-27-68

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I/We do hereby declare that I am/we are in possession of an invention the title of which is

"AGENTS FOR REMOVING DANDRUFF"

I am/We are the assignee(s)/legal representative(s) of the inventor(s). Application(s) for protection for the invention has/have been made in the following country/countries and on the following official dates i.e.:—

| | | | | |
|---|---|---|---|---|
| 1. (country) | Germany | (date) | 14th February, 1967 | (number) Sch 40 231 IV a/30 |
| 2. (country) | | (date) | | (number) |
| 3. (country) | | (date) | | (number) |

The said application or each of the said applications was the first application in a convention country in respect of the relevant invention by me/us or by any person from whom I/we derive title. To the best of my/our knowledge and belief there is no lawful ground for objection to the grant of a patent to me/us on this application. I/We pray that a patent be granted to me/us for the invention in priority over other applicants and that such patent shall have the official date of the first application in a convention country i.e. 14th February, 1967.

I/We hereby appoint the partners and qualified staff of the firm of ADAMS & ADAMS, jointly and severally, to act for me/us in all matters relating to this application and any letters patent granted thereon.

Dated this 13th day of February, 196[illegible]

Address for service:
C/o ADAMS & ADAMS,
ALLIED BUILDING,
PRETORIA.

| Table of Classification | |
|---|---|
| Class | Sub-class |
| 167 | 87 |

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PA[illegible] ATTORNEY

Signature of Applicant/s and Capacity

A. & A. Ref. No. 5704.

PATENTS

FORM NO. 3

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SOUTH AFRICA SOUTH AFRICA

REPUBLIC OF SOUTH AFRICA

The Patents Act, 1952

# COMPLETE SPECIFICATION

680962

Here insert (in full) name, address of applicant(s) as in application form.

(a) HANS SCHWARZKOPF, a German Kommanditgesellschaft organized and existing according to the laws of the Federal Republic of Germany, of Hohenzollernring 127-129, 2000 HAMBURG 50, Germany.

Here insert title (verbally agreeing with that in the application form.)

(b) "AGENTS FOR REMOVING DANDRUFF"

I/WE do hereby declare this invention, the manner in which and the method by which it is to be performed, to be particularly described and ascertained in and by the following statement:-

The invention relates to an agent for removing and preventing the formation of dandruff by utilising 5,7-dichloro-8-hydroxy-quinoline or its salts in combination with shampoos or hair-conditioning bases.

The human skin continuously builds itself anew and expells parts of the old skin. These skin particles, referred to as flakes, are not recognisable with the naked eye in the case of normal flake formation. Also the formation of flakes by the skin of the head, i.e. dandruff, takes place practically invisibly in normal cases. In many cases, more particularly on the skin of the head, the dandruff formation takes place with the formation of large-surface formations, perceptible with the naked eye and definitely embarrassing, more particularly from the cosmetic point of view. When combing the hair, the dandruff falls on the clothing and gives the impression of lack of hygiene. consequently, one of the purposes of hair cosmetics is to prevent the formation of visible dandruff. Many agents have already been suggested for this purpose, for example bacteriostatic and fungistatic substances. Such substances are, for example, phenols, resorcin, hexa-chlorophene or 2,2'-thio-bis-4,6-dichloro-phenol, carbanilides such as for example 3,4,4'-trichloro-salicyl-anilide, quaternary ammonium compounds such as cetyl-trimethyl-ammonium bro[illegible] organic metal compounds such as for example phenyl-[illegible] acetate, hydroxy-quinolines such as for example 5-iod[illegible] hydroxy-quinoline or 5-chloro-7-iodine-8-hydroxy-quinoline, pyridine-thionines such as 2-pyridine-thionine-N-oxide, more particularly its zinc salt, N-trichloromethyl-mer[illegible] 4-cyclo-chloro-hexene-1,2-carboximide, dialkyl-[illegible] dicarbonic acids such as for example the disulph[illegible] beta-mercapto-propionic acid and undecylenic acid-[illegible]

It was supposed that there was a connection between the flora of bacteria on the skin of the head and the occurrence of visible dandruff. More recent works showed that these findings are very doubtful because there are no clear differences in the bacteria flora of the skin of the head in the case of normal invisible dandruff. The action of some bacteriostatic or fungistatic active substances against visible dandruff can therefore, with the known state of technique, not simply be explained with the abovementioned properties of these substances. That also other conditions for an effective activity against visible dandruff exist is proved by the activity of sulphur, sulphur compounds and selene compounds against dandruff. Sodium selenite, an active agent against dandruff, hardly shows any bacteriostatic effect. This is evident from Table I. In this Table the threshold dilution is given in γ/ml, in which, in aqueous solution, no checking of germination is observed.

TABLE I

| | Staph. Aureus "Oxford" | Escherichia | Candida albicans |
|---|---|---|---|
| Sodium selenite | 500 | 500 | 500 |
| Cetyl-trimethyl-ammonium bromide | 2 | 1.5 | |

As a comparison with sodium selenite, the bacteriostatic effect of cetyl-trimethyl-ammonium bromide is indicated in Table I.

The determination of the bacteriostatic threshold effect was ascertained with the test tube batter[illegible] test.

The activity of the above substances, hardly bacteriostatically active, against the formation of dandruff is often attributed to their keratolytic action. There is however no exact data in this respect, so that no correct indication of the mechanism of the activity of these compounds against the formation of dandruff can be given.

It was surprisingly found that, among the large number of bacteriostatically and fungistatically active chemical compounds, there are such which, apart from this effect, show a specific activity against dandruff. It concerns the compound 5,7-dichloro-8-hydroxy-quinoline and its salts. These compounds meet all requirements expected from an active substance for hair-cosmetic agents for combating dandruff, be they hair washing agents or so-called hair cures.

Such requirements are:

Constant activity with storing for long periods, more particularly in the presence of wash-active substances as incorporated in shampoos or hair cures.

Substantivity of the active substances on the skin of the head and on the hair for ensuring a permanent activity between the hair washes or between the cure treatments.

A satisfactory hair tolerance and, finally, tolerance with all substances used for formulating shampoos and hair cures.

The maintenance of the full bacteriostatic activity with storing for long periods and in the presence of wash-active substances was proved by the test tube battery dilution test. The values in Table II show a very bacteriostatic effect of 5,7-dichloro-8-hydroxy-quinoline and

| | | Staphylococcus epidermidis | Corynebact. pseudodiphth. | Escherichia coli | Pityrosporon ovale | |
|---|---|---|---|---|---|---|
| | No curbing | No curbing | No curbing | No curbing | No curbing | No curbing |
| 1:10 | 1:2[1] | No curbing | 1:4 | No curbing | No curbing | 1:2 |
| A<br>-dichloro-8-<br>-quinoline<br>1:10 | 1:256 | 1:512 | 1:1024 | 1:256 | 1:512 | 1:512 |
| B<br>7-dichloro-8-<br>-quinoline<br>1:10 | 1:128 | 1:512 | 1:512 | 1:2 | 1:512 | 1:512 |
| A<br>muth salt of<br>loro-3-hydroxy-<br>e diluted 1:10 | 1:256 | 1:256 | 1:1024 | 1:512 | 1:256 | 1:512 |
| B<br>alt of 5,7-<br>o-3-hydroxy-<br>e diluted 1:10 | 1:512 | 1:512 | 1:1024 | 1:512 | 1:256 | 1:256 |
| A<br>otorosan[2]<br>1:10 | 1:64 | 1:16 | 1:16 | 1:8 | 1:8 | 1:16 |
| B<br>otorosan<br>1:10 | 1:16 | 1:8 | 1:8 | 1:16 | 1:8 | 1:16 |

of

1) The figures indicate up to which dilution/the 1:10 diluted solvents there is no growth of the cultures (the non-diluted hairwash solutions do not show a clear sudden change of the indicator).

2) 2,2'-thio-bis-(4,4'-chlorophenol)

Hairwash A:

1.0 % lecithin
0.3 % stearic acid
0.3 % palmitic acid
0.1 % oleic acid
4.0 % oleic acid diethanolamide
8.0 % sodium salt of the condensation product from cocoanut oil acid and Sarkosin
2.0 % glycerin
1.0 % Turkey red oil
70.0 % sodium salt of the condensation product of fatty acid and methyl-taurin (45-49%)
6.0 % sodium salt of the condensation product of stearic acid and methyl-taurin (50%)
0.6 % perfume
6.7 % desalted water

Hairwash B:

20.0 % Lamepon S (potassium salt of a fatty acid - albumin condensate) (35-36%)
40.0 % Texapon N (fatty alcohol ether sulphate - sodium salt - 28%)
5.0 % Medialan KF (condensation product of cocoan oil acid and Sarkosin, neutralised with organic bases - 40%)
0.5 % perfume
34.5 % desalted water.

Contrary to this, the Bakterosan (2,2'-thio-bis-4,4'-chlorophenol) known as a dandruff factor, loses its effect in the same hairwash as is clearly shown in Table III. In a solution of dimethyl-sulphoxide, 2,2'-thio-bis-4,4'-chlorophenol shows only a slightly weaker effect than 5,7-dichloro-8-hydroxy-quinoline and its salts.

TABLE III

| | Isoconazole | Staphylococcus epidermidis | Corynebacterium pseudodiphtheriticum | Escherichia coli | Pityrosporon ovale | |
|---|---|---|---|---|---|---|
| ...-(2,4-dichlorobenzyl)-...-dimethyl- | 1,56[2] | 6,25 | 0,39 | 62,5 | 3,9 | 7,8 |
| ...-3-hydroxy-...-dimethyl- | 6,25 | 0,78 | 3,12 | 7,8 | 1,9 | 1,9 |

...io-bis-(4,4'-chlorophenol) 2) limit effect concentration in γ/ml

TABLE IV

| | | | | | | |
|---|---|---|---|---|---|---|
| ...-dichloro-8-...inoline, freshly ...:10 diluted | 1:128 | 1:512 | 1:512 | 1:512 | 1:512 | 1:512 |
| ...-dichloro-8-...inoline, stored ... at 40°C, ... with water | 1:128 | 1:512 | 1:1024 | 1:512 | 256 | 1:512 |
| ...uth salt of ...oro-8-hydroxy-..., freshly prepared, ...d with water. | 1:256 | 1:256 | 1:1024 | 1:512 | 1:256 | 1:512 |
| ...uth salt of ...oro-8-hydroxy-... at 4°C, ... stored 6 months, ...ed with water. | 1:256 | 1:128 | 1:1024 | 1:256 | 1:256 | 1:512 |

...ssive the limit dilution of the growth curb, starting from the hairwash 1:10 diluted with water. The dilution ...irwash was carried out immediately before the testing. The composition of the hairwashes are shown in Table II.

As shown in Table IV, the action of the compounds according to the invention is not lost even after storing for 6 months at 40°C.

The substantivity and, consequently, the effect of 5,7-dichloro-8-hydroxy-quinoline and its salts, present after a long period, [illegible] the identification of germs on the hair. It was found that, with the removal of 10 separate hairs of a test person, there were the same cultures as with the removal of 100 hairs of the same test person. With the removal of about 10 hairs it could be taken for certain that practically all cultures occurring on the hair were included.

In the tests, 10 hairs were always used. The hairs were removed 0,5 cm at the maximum from the skin of the head, cut off with sterile scissors, transferred with a sterile pipette into a sterile test tube and, finally, placed on a nutritive medium. After incubating for 24 hours at 37°C it was transferred to blood agar plates which again were incubated for 24 hours at 37°C. Thereafter the cultures were determined qualitatively. Table V shows the results of these tests.

| | Sampling before washing | Sampling immediately after washing | Sampling 3 hours after washing | Sampling 24 hours after washing |
|---|---|---|---|---|
| Test person 1 washed with hair-[illegible] without addition. | Staph.epider-mis; Staph. albus haem | Staph.epider-mis | Staph. epi-dermis; Streptococci turning green | Staph. epi-dermis; Staph. albus haem; gramnegative rods (dirt germs) |
| Test person 2 washed with hair-[illegible] without addition. | Staph. albus haem; Staph. epidermis | Staph. albus haem; Staph. epidermis | Staph. albus haem; Staph. aureus haem Staph. epi-dermis | Staph. albus; Staph. aureus haem; Staph. epidermis |
| Test person 3 washed with hair-[illegible] without addition. | Staph. albus haem; gram-negative rods (dirt germs) | Staph. albus haem. | Staph. albus haem; Staph. aureus haem; gramnegative rods (dirt germs) | Staph. albus haem; Staph. aureus haem; gramnegative rods (dirt germs) |
| Test person 4 washed with hair-[illegible] without addition. | Aerobacter aerogenes; Staph. epi-dermis. | Staph. citreus | Aerobacter aerogenes; Staph. epi-dermis. | Aerobacter aerogenes; Staph. epider-mis |
| Test person 5 washed with hair-[illegible] without addition. | Bacillus cereus;Staph. albus haem. | Staph. albus haem. | Staph. albus haem; Staph. epidermis; pseudonomas. | Staph. albus haem; Staph. epidermis; pseudonomas. |
| Test person 6 washed with hair-[illegible] + 2% cal-cium salt of 5,7-dichloro-8-hydroxy-quinoline. | Staph. albus haem; Strept. anh. | - | Staph. albus haem. | Staph. albus haem. |
| Test person 7 washed with hair-[illegible] + 2% cal-cium salt of 5,7-dichloro-8-hydroxy-quinoline. | Staph. albus; Strept.anh; aerobacter aerogenes. | Staph.albus haem. | Staph. albus haem. | Staph. albus haem. |
| Test person 8 washed with hair-[illegible] + 2% cal-cium salt of 5,7-dichloro-8-hydroxy-quinoline. | Staph. albus haem; Esch. coli. | - | Staph. albus haem. | Staph. albus haem. |
| Test person 9 washed with hair-[illegible] + 2% cal-cium salt of 5,7-dichloro-8-hydroxy-quinoline. | Staph. albus haem; aerobe haem. Actinomyceten. | Staph. albus haem. | Staph. albus haem. | [illegible] |
| Test person 10 washed with hair-[illegible] + 2% cal-cium salt of 5,7-dichloro-8-hydroxy-quinoline. | Staph. albus haem; Klebs. spec. | Staph. albus haem. | Staph. albus haem. | [illegible] |

TABLE V continued

| | Sampling before washing | Sampling immediately after washing | Sampling 3 hours after washing | Sampling 24 hours after washing. |
|---|---|---|---|---|
| [illegible] person 11 [illegible] with [illegible] wash A + 2% [illegible] salt of [illegible]-dichloro-8-[illegible]-quinoline. | Staph. albus haem; gram-negative rods (air germs) | - | Staph. albus haem. | Staph. albus haem. |
| [illegible] person 12 [illegible] with [illegible] wash A + 2% [illegible] salt of 5,7-dichloro-8-hydroxy-quinoline. | Gramnegative rods (dirt germs); Streptococci turning green; Staph. alb. haem; Sarcina lutea. | Staph. albus haem. | Staph. albus haem. | Staph. albus haem. |
| [illegible] person 13 [illegible] with [illegible] wash A + 2% [illegible] salt of [illegible]-dichloro-8-hydroxy-quinoline. | Staph. albus haem; Bac. cereus. | Staph. albus haem. | Staph. albus haem. | Staph. albus haem. |

The compositions of the hairwashes A and B are given in Table III.

The hair samples were taken before the washing, immediately after washing and 3 hours and 24 hours after the washing.

With the heads washed with the hairwash containing the calcium salt of 5,7-dichloro-8-hydroxy-quinoline according to the invention, there was throughout a slower reinfestation than with the hairwashes, used for comparison, without the addition according to the invention.

The tolerance of the hair to the compounds according to the invention is very good. By means of the "repeated-insult-patch-test" it was proved that shampoos and hair cures with 2% content of the active principles according to the invention there is no sensitising.

The tolerance of the active principles according to the

and hair cures, is beyond doubt. With the working-in of the active principle it is recommended to make use of particularly finely ground products. The uniform distribution of the active principles can, furthermore, be improved by additions of, for example, polyethylene oxides, ethylene oxide enriching products and/or methylcellulose.

The practical application of the shampoos or hair cures containing the active principles according to the invention, is carried out as usual. In the case of heavy dandruff a hairwash at intervals of 2 - 3 days is recommended. The washing of the hair can be followed by a treatment with an agent containing the active principles. Proof of the satisfactory activity of the substances according to the invention is best given by a controlled treatment of the test persons by the hairdresser. It is particularly convincing to conduct tests on one side of the head, which tests enable the expert, often already after a few washings, to make a clear distinction between the differently treated halves of the head. The agent according to the invention is applied as follows:

0.05 to 5.0, preferably 0.5 to 2.0% of 5,7-dichloro-8-hydroxy-quinoline or a salt of this compound are worked into a shampoo formulation. With heavy dandruff, a head washing is carried out every third or fourth day. [illegible] fourth or fifth washing the dandruff disappeared in practically all cases. So as to prevent the recurrence of [illegible] a washing with the dandruff shampoo weekly or fortnightly is sufficient in general. In particularly persistant [illegible] it is recommended to treat the hair, after the washing, [illegible] a curative agent containing one of the active principles according to the invention.

For a more detailed description of the [illegible] of the substances active against dandruff, the following [illegible] are given:

EXAMPLE 1.

20 persons, suffering from heavy dandruff, were given a hairwash every third or fourth day with a dandruff shampoo consisting of:

| | |
|---|---|
| Lecithin | 1.0% |
| Stearic acid | 0.3% |
| Palmitic acid | 0.3% |
| Oleic acid | 0.1% |
| Oleic acid diethanolamide | 4.0% |
| Sodium salt of the condensation product from cocoanut oil acid and sarkosin | 8.0% |
| Glycerin | 2.0% |
| Turkey red oil | 1.0% |
| 5,7-dichloro-8-hydroxy-quinoline | 1.0% |
| Sodium salt of the condensation product from $C_{12}$-fatty acid and methyl taurin (45-49% of active substance) | 69.0% |
| Sodium salt of the condensation product from stearic acid and methyl taurin (50% of active substance). | 6.0% |
| Perfume | 0.6% |
| Desalted water | 6.7% |
| | 100.0% |

After the washing, the hairwas thoroughly rinsed. As a comparison, 20 hair washings were carried out with the same formulation without the addition of 5,7-dichloro-8-hydroxy-quinoline every third to fourth day.

With the third hairwash, there were already some advantages with the heads washed with the shampoo containing active substance. After washing five times, of 20 heads sixteen were practically free from dandruff. The other 4 showed much less dandruff than at the beginning of the test washes. The blind test [illegible] improvement. Repeated washing with a shampoo

without the addition of 5,7-dichloro-8-hydroxy-quinoline did not lead to a decrease or disappearance of dandruff. From among the persons treated with the shampoo containing active principles, a group of 8 persons were thereafter treated at intervals of three to four days with the shampoo without active principle, while another group of 8 persons were further treated with the dandruff shampoo, containing active principle, at intervals of three to four days. After five to ten washings, there was a reinfestation with dandruff in the 8 persons treated with the formulation without the addition of active principle, while the persons treated with the shampoo containing active principle remained free from dandruff.

EXAMPLE 2

Bismuth salt of 5,7-dichloro-8-hydroxy-quinoline was used as active principle. The shampoo formulation corresponded to the formulation of Example 1. 2.0% of the active principle were used, while the quantity of water added was reduced to 5.7%.

The hair of 20 persons, suffering from heavy dandruff, was washed at one side with the above dandruff shampoo, containing active principles, and at the other side with the same formulation without the addition of the active principle. After four head washings at intervals of three to four days, the side washed with the dandruff shampoo containing the active principle showed a clear improvement. The dandruff was reduced. After eight washings, practically all halves washed with the dandruff shampoo containing the active principle were free from dandruff, while the halves washed with the same formulation without the addition of active principle did not show any improvement.

EXAMPLE 3.

Use was made of a dandruff shampoo of the formulation:

| | |
|---|---|
| calcium salt of $C_{12}$-fatty acid-albuman-condensate (35-36% of active substance). | 20% |
| sodium salt of lauryl-alcohol-ether sulphate (28% of active substance). | 40.0% |
| Condensation product from cocoanut oil acid and sarkosin, neutralised with organic bases. (47% of active substance) | 5.0% |
| Perfume | 0.5% |
| Calcium salt of 5,7-dichloro-8-hydroxy-quinoline | 1.0% |
| Desalted water | 43.5% |

For comparison use was made of a shampoo of the same formulation, without the addition of active substance. The washings were carried out at one side with the shampoo containing active substance and at the other side with shampoo without active substance. 18 persons took part in this test. After three washings at intervals of 3 to 4 days, there were already clear differences between the two halves. After six washings, 15 of the halves washed with shampoo containing the active substance were practically free from dandruff, while the halves washed with shampoo without active substance remained without change. With the remaining three heads there was an improvement at the side washed with shampoo containing the active substance as compared with the initial state. The halves washed with shampoo without active substance addition were practically unchanged as compared with the initial findings, as regards dandruff.

EXAMPLE 4

After a washing with shampoo without active substance addition as in Example 1 and 2, a hair cure of the formulation

| | |
|---|---|
| Cetyl alcohol | 9.2% |
| Stearyl alcohol | 9.0% |
| Cetyl palmitate | 3.0% |
| Paraffin oil | 2.0% |
| Sodium salt of ethoxylated cocoanut oil alcohol sulphates | 3.0% |
| Sorbit | 2.0% |
| Wheat germ oil | 0.1% |
| Calcium salt of 5,7-dichloro-8-hydroxy-quinoline | 1.0% |
| Desalted water | 70.0% |

was massaged into the hair and rinsed out after 10 minutes. This treatment was carried out by the hairdresser on 10 test persons with heavy dandruff. For comparison, 10 test persons were treated with the same formulation without the addition of active substance. The treatment was repeated every three to four days. After three treatments, five of the persons treated with the hair cure containing active substance showed only very little dandruff. The remaining five test persons treated with hair cure containing active substance showed a clear decrease of dandruff. The 10 test persons treated with the hair cure without addition of the active substance according to the invention all showed only a small decrease of the dandruff.

After six treatments with the hair cure containing the active principle according to the invention, 8 persons were free from dandruff, while 2 persons showed very little dandruff.

From among 10 test persons treated with the hair cure without the active substance according to the invention, three showed a considerable decrease of dandruff, seven only a small decrease of dandruff after six treatments.

Having now particularly described and ascertained our said invention and the manner in which the same is to be performed, we declare that what we claim is:

1. Agents for removing dandruff, characterised by a content of 0.1% to 5.0%, preferably 0.5% to 2.0%, of 5,7-dichloro-8-hydroxy quinoline and/or one of its salts, in shampoo bases known per se, or hair conditioning agents.

2. Agents for removing dandruff, substantially as described herein.

3. A method of removing dandruff, which comprises applying to the head and/or hair an agent as claimed in claim 1 or claim 2.

Dated this 13th day of FEBRUARY 1968